Treatment of Deep Vein Thrombosis and Pulmonary Embolism

An Educational Slide Set

American Society of Hematology 2020 Guidelines for Management of Venous Thromboembolism

Slide set authors:
Zachary Liederman MD MScCH (University of Toronto)
Eric K. Tseng MD MScCH (University of Toronto)
Thomas L. Ortel MD PhD (Duke University)
Clinical Guidelines

American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism

ASH Clinical Practice Guidelines on VTE

1. Prevention of VTE in Surgical Hospitalized Patients
2. Prevention of VTE in Medical Hospitalized Patients
3. **Treatment of Acute VTE (DVT and PE)**
4. Optimal Management of Anticoagulation Therapy
5. Prevention and Treatment of VTE in Patients with Cancer
6. Heparin-Induced Thrombocytopenia (HIT)
7. Thrombophilia
8. Pediatric VTE
9. VTE in the Context of Pregnancy
10. Diagnosis of VTE
11. Anticoagulation in Patients with COVID-19
12. Adaptation of ASH Management of VTE Guidelines for Latin America
How were these ASH guidelines developed?

**PANEL FORMATION**
Each guideline panel was formed following these key criteria:
- Balance of expertise (including disciplines beyond hematology, and patients)
- Close attention to minimization and management of conflicts of interest

**CLINICAL QUESTIONS**
20 to 30 clinically-relevant questions generated in PICO format (population, intervention, comparison, outcome)

**EVIDENCE SYNTHESIS**
Evidence summaries incorporated into Evidence to Decision (EtD) frameworks, which also addressed:
- Resource use
- Feasibility
- Acceptability
- Equity
- Patient values and preferences

**Example: PICO question**
“Should thrombolytic therapy in addition to anticoagulation vs. anticoagulation alone be used for patients with extensive proximal DVT?”

**MAKING RECOMMENDATIONS**
Recommendations made by guideline panel members based on EtD frameworks.
How patients and clinicians should use these recommendations

<table>
<thead>
<tr>
<th>STRONG Recommendation</th>
<th>CONDITIONAL Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>(&quot;The panel recommends...&quot;)</td>
<td>(&quot;The panel suggests...&quot;)</td>
</tr>
</tbody>
</table>

**For patients**
- Most individuals would want the intervention.
- A majority would want the intervention, but many would not.

**For clinicians**
- Most individuals should receive the intervention.
- Different choices will be appropriate for different patients, depending on their values and preferences. Use shared decision making.
Grading the quality of evidence

- Low (or Very Low)
- Moderate
- Strong
Objectives

By the end of this session, you should be able to

1. Describe the *initial management* of patients with deep vein thrombosis (DVT) and pulmonary embolism (PE)

2. Describe recommendations for *duration of anticoagulation* after venous thromboembolism (VTE)

3. Describe recommendations for management of *recurrent VTE*
VTE (including DVT and PE) occurs in 1-2 per 1,000 people per year

One third of patients with newly diagnosed VTE present with PE

For patients with unprovoked VTE, risk of recurrence after completing a primary treatment course of anticoagulation is about 10% in two years

The incidence of VTE increases with age – as high as 1 in 100 in individuals above 80 years old

VTE is a common and important cause of morbidity and mortality
These guidelines

These guidelines are about managing VTE during:

• Initial stages (within 2 weeks)
• Primary treatment (3-6 months)
• Secondary prevention (beyond 6 months)
Case 1: Unprovoked DVT

48 year old male

Medical History: None

Medications: None

Seen in the Emergency Department with: left leg pain and swelling x 24 hours

Heart rate 80 beats per min
Respiratory rate 16 breaths per min
Oxygen saturation 99% on room air
Blood pressure 130/80
(+): Left calf swelling

D-dimer: 2,500 mcg/ml

Leg US: distal external iliac vein, superficial femoral and popliteal vein non-compressible (occlusive DVT)
What initial management plan would you recommend:

A. Anticoagulation only
B. Thrombolysis in addition to anticoagulation
C. Compression stockings in addition to anticoagulation
D. IVC filter insertion in addition to anticoagulation
Recommendation

In most patients with proximal DVT, the panel suggests anticoagulation therapy alone over thrombolytic therapy in addition to anticoagulation (conditional recommendation, low certainty)

Thrombolytic therapy + Anticoagulation compared with Anticoagulation alone in patients with extensive proximal DVT:

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Risk with Anticoagulation</th>
<th>Risk difference with thrombolytic therapy + anticoagulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>0.77 (0.26-2.28)</td>
<td>9 per 1,000</td>
<td>2 fewer deaths per 1,000</td>
<td>2 fewer deaths per 1,000 (7 fewer to 12 more)</td>
</tr>
<tr>
<td>PTS</td>
<td>0.71 (0.60 to 0.085)</td>
<td>641 per 1,000</td>
<td>186 fewer PTS per 1,000</td>
<td>186 fewer PTS per 1,000 (96 fewer to 253 more)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1.85 (1.41 to 2.44)</td>
<td>36 per 1,000</td>
<td>31 more bleeds per 1,000</td>
<td>31 more bleeds per 1,000 (15 fewer to 52 more)</td>
</tr>
</tbody>
</table>

Remarks:
Patients with limb threatening DVT may require thrombolysis

Quality of Evidence (GRADE): Low ⬜️ Moderate ⬜️ Strong ⬜️
Recommendation

For patients with DVT including those at increased risk of PTS, the panel *suggests against* the use of compression stockings (conditional recommendation, low certainty)

**Anticoagulation alone** compared with **compression stockings and anticoagulation** in patients with extensive DVT:

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk with VKA</td>
</tr>
<tr>
<td>• Mortality</td>
<td>0.99 (0.72-1.36)</td>
<td>46 per 1,000</td>
</tr>
<tr>
<td>• PE</td>
<td>0.72 (0.31-1.70)</td>
<td>15 per 1,000</td>
</tr>
<tr>
<td>• DVT</td>
<td>0.56 (0.12 to 2.70)</td>
<td>40 per 1,000</td>
</tr>
<tr>
<td>• PTS</td>
<td>0.62 (0.38 to 1.01)</td>
<td>213 per 1,000</td>
</tr>
</tbody>
</table>

Remarks:
Stockings may still be considered for symptomatic relief in select patients
Treatment beyond anticoagulation for prevention of Post Thrombotic Syndrome (PTS)

• PTS may develop in 30% to 50% patients (5% to 10% severe)

• Adjunctive therapies can include compression stockings and thrombolysis:
  o Trend towards decreased PTS but not significant
  o No impact on mortality
  o For thrombolysis – increased bleeding risk

• There remains low certainty in the evidence and therapy may be considered for patients with:
  o Low risk of bleeding (thrombolysis)
  o Value rapid resolution of symptoms and prevention of PTS
**Recommendation**

In patients with VTE, the panel *suggests* using **DOACs over VKAs** (conditional recommendation, moderate certainty)

**DOAC** compared with **VKA** for VTE:

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk with VKA</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.99 (0.85-1.15)</td>
<td>39 per 1,000</td>
</tr>
<tr>
<td>PE</td>
<td>0.97 (0.77-1.23)</td>
<td>20 per 1,000</td>
</tr>
<tr>
<td>DVT</td>
<td>0.80 (0.59 to 1.09)</td>
<td>26 per 1,000</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>0.63 (0.47 to 0.84)</td>
<td>17 per 1,000</td>
</tr>
</tbody>
</table>

**Remarks:**
May not be appropriate for all patient populations

The panel does not suggest one DOAC over another

Quality of Evidence (GRADE): Low • Moderate • Strong •
Recommendation

For patients with **uncomplicated DVT**, the ASH guideline panel *suggests* offering **home treatment** over hospital treatment (conditional recommendation, low certainty)

**Home treatment** compared with **hospital treatment** in patients continuing on indefinite anticoagulation

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk with hospital treatment</td>
</tr>
<tr>
<td>Mortality (10 days)</td>
<td>Not estimable</td>
<td>4 per 1,000</td>
</tr>
<tr>
<td>PE</td>
<td>0.64 (0.44 to 0.93)</td>
<td>68 per 1,000</td>
</tr>
<tr>
<td>DVT</td>
<td>0.61 (0.42 to 0.90)</td>
<td>74 per 1000</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>0.67 (0.33 to 1.36)</td>
<td>19 per 1,000</td>
</tr>
</tbody>
</table>

**Remarks:**
Hospital treatment may benefit patients with limb threatening DVT or those at high risk of bleeding
Case: back to our patient

Uncomplicated unprovoked VTE in previously well patient

• Initial management:
  o Anticoagulation only (no thrombolysis, no compression stockings, no IVC filter)
  o DOAC over VKA
  o Home treatment over hospital treatment
The patient receives 6 months of anticoagulation for primary treatment. What duration of anticoagulation do you recommend for secondary prevention?

A. 6-12 months
B. No secondary prevention is required
C. Indefinite
D. Will depend on use of prognostic scores
Recommendation

After primary treatment for patients with unprovoked DVT or PE, the panel suggests indefinite antithrombotic therapy (conditional, moderate certainty)

Indefinite anticoagulation compared with stopping anticoagulation in patients with unprovoked VTE after primary treatment:

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk with stopping</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.75 (0.49-1.13)</td>
<td>18 per 1,000</td>
</tr>
<tr>
<td>PE</td>
<td>0.29 (0.15 to 0.056)</td>
<td>29 per 1,000</td>
</tr>
<tr>
<td>DVT</td>
<td>0.20 (0.12 to 0.34)</td>
<td>63 per 1,000</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>2.17 (1.40 to 3.35)</td>
<td>5 per 1,000</td>
</tr>
</tbody>
</table>

Remarks:
Does not apply to patients who are at high risk of bleeding complication

Quality of Evidence (GRADE): Low ◯ Moderate ◯ Strong ◯
Recommendation

For patients with unprovoked DVT and/or PE, the panel suggests against routine use of prognostic scores, D-Dimer testing or ultrasound to guide the duration of anticoagulation (conditional, low certainty).

### Prognostic Scores
- HERDOO2
- VIENNA
- DASH

### D-Dimer Testing
- Persistently elevated D-Dimer

### U/S
- Residual vein thrombus

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Standard risk</td>
</tr>
<tr>
<td>N/A: Insufficient evidence for treatment outcomes based on prognostic tools compared to standard approach</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Recommendation

For patients with DVT and/or PE who will continue with a DOAC for secondary prevention, the panel suggests using standard-dose DOAC or lower-dose DOAC (conditional recommendation, moderate certainty)

**Lower-dose** compared with **standard-dose DOAC** in patients continuing on indefinite anticoagulation

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Risk with standard dose</td>
<td>Risk difference with reduced dose</td>
</tr>
<tr>
<td></td>
<td>Risk with standard dose</td>
<td>DOAC</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.68 (0.10-4.57)</td>
<td>6 per 1,000</td>
</tr>
<tr>
<td>PE</td>
<td>1.25 (0.54 to 2.91)</td>
<td>5 per 1,000</td>
</tr>
<tr>
<td>DVT</td>
<td>0.75 (0.36 to 1.53)</td>
<td>9 per 1000</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>0.97 (0.34 to 2.80)</td>
<td>4 per 1,000</td>
</tr>
</tbody>
</table>

Quality of Evidence (GRADE): Low 🟥 Moderate 🟢 Strong ❌

Lower dose DOAC regimens for secondary prevention of VTE
- Apixaban 2.5 mg BID
- Rivaroxaban 10 mg OD
Case Conclusion

Uncomplicated unprovoked VTE in previously well patient

- Initial management:
  - Anticoagulation only (no thrombolysis, no compression stockings, no IVC filter)
  - DOAC over warfarin
  - Home treatment over hospital treatment

- Duration:
  - Indefinite antithrombotic therapy
  - Standard or reduced dose DOAC
Case 2: Provoked DVT and PE (transient risk factor)

76 year old male

**Medical History:** CAD (MI 5 years earlier), HTN, Type 2 Diabetes

**Medications:** ASA, Amlodipine, Metformin, Rosuvastatin

**Seen in the Emergency Department with:** SOB and right leg pain x 48 hours. Underwent total hip replacement 1 week earlier and has not been taking prescribed DVT prophylaxis.

Heart rate 90 beats per min  
Respiratory rate 22 breaths per min  
Oxygen saturation 99% on RA  
Blood pressure 150/90  
(+ ) Right calf swelling

**Right Leg US:** superficial femoral and popliteal vein non-compressible (occlusive DVT)

**CTPA:** Pulmonary embolism involving segmental arteries of the left lower lobe
Recommendations

IVC filter insertion is not routinely recommended unless there is a contraindication to anticoagulation.

For patients with proximal DVT and significant pre-existing cardiopulmonary disease, as well as for patients with PE and hemodynamic compromise, the panel suggests anticoagulation alone rather than anticoagulation plus insertion of an IVC filter (conditional recommendation, low certainty).

**IVC filter in addition to anticoagulation versus anticoagulation alone (NO FILTER):**

<table>
<thead>
<tr>
<th>Outcomes (Quality of Evidence)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Risk difference using FILTER</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Risk with NO FILTER</td>
<td>Risk difference</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RR 1.15 (0.83 to 1.60)</td>
<td>60 per 1000</td>
<td>9 more death per 1,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(10 fewer to 36 more)</td>
</tr>
<tr>
<td>Mortality</td>
<td>RR 0.54 (0.22 to 1.33)</td>
<td>5 per 1000</td>
<td>2 fewer PE per 1,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(4 fewer to 2 more)</td>
</tr>
<tr>
<td>PE</td>
<td>RR 1.64 (0.93 to 2.90)</td>
<td>5 per 1,000</td>
<td>3 more DVT per 1,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0 fewer to 10 more)</td>
</tr>
</tbody>
</table>

If IVC filter is inserted (e.g., high bleeding risk) a retrievable filter is recommended with removal once patient can safely receive anticoagulant therapy.
Recommendation

For patients with DVT and/or PE with stable CVD, previously taking aspirin the panel suggests suspending aspirin for the duration of anticoagulation therapy (conditional, very low certainty)

**Suspending ASA (Anticoagulation alone) compared with Continuing ASA (ASA + anticoagulation)**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major bleeding</td>
<td>1.26 (0.34 to 2.80)</td>
<td>Risk with stopping ASA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>29 per 1,000</td>
</tr>
</tbody>
</table>

**Remarks:**
Does not apply to patients with recent coronary event or coronary intervention
**Recommendation**

In patients with pulmonary embolism (PE) with low risk of complications, the panel *suggests* home treatment over hospital treatment (conditional recommendation, very low certainty)

**Home treatment** compared with **hospital treatment** in patients continuing on indefinite anticoagulation

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk with hospital treatment</td>
<td>Risk difference with home treatment</td>
</tr>
<tr>
<td>Mortality (30 days)</td>
<td>0.33 (0.01 to 7.98)</td>
<td>4 per 1,000</td>
<td>3 fewer deaths per 1,000 (4 fewer to 30 more)</td>
</tr>
<tr>
<td>PE</td>
<td>2.95 (0.12 to 71.85)</td>
<td>0 per 1,000</td>
<td>0 fewer PE per 1,000 (0 fewer to 0 fewer)</td>
</tr>
<tr>
<td>DVT</td>
<td>Not estimable</td>
<td>0 per 1000</td>
<td>Not estimable</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>6.88 (0.36 to 132.14)</td>
<td>0 per 1,000</td>
<td>0 fewer bleeds per 1,000 (0 fewer to 0 fewer)</td>
</tr>
</tbody>
</table>

**Remarks:**
Hospital treatment may benefit patients with submassive or massive PE, a high risk for bleeding or requiring IV analgesics

Quality of Evidence (GRADE): Low 🟥 Moderate 🟡 Strong 🟢
Case: back to our patient

Provoked DVT and PE (transient risk factor) in patient with cardiopulmonary disease

• Initial management:
  o Anticoagulation only (no thrombolysis, no compression stockings, no IVC filter)
  o DOAC over warfarin
  o Suspend ASA
  o Home treatment over hospital treatment

The patient is shocked that this happened to him and asks what caused his blood clot.
Provoking Risk Factors for VTE

**Transient Risk Factors**
(resolve after provoked VTE)

**MAJOR Risk Factor (occurs within 3 mth)**
- Surgery, gen anesthesia > 30 min
- Confined to hospital bed ≥ 3 days with acute illness
- Cesarean section

**MINOR Risk Factor (occurs within 2 mth)**
- Estrogen therapy (OCP, HRT)
- Pregnancy, puerperium
- Confined to bed out of hospital ≥ 3 days with acute illness
- Leg injury, reduced mobility ≥ 3 days

**Chronic (Persistent) Risk Factors**
(persistent after VTE occurs)

- Active cancer (ongoing chemo; recurrent or progressive disease)
- Inflammatory bowel disease
- Autoimmune disorder (e.g., antiphospholipid syndrome, rheumatoid arthritis)
- Chronic infection
- Chronic immobility (e.g., spinal cord injury)
The patient recovers well in hospital and is ready for discharge. In the absence of any major bleeding concerns, for how long should this patient be treated with anticoagulation?

A. 3-6 months
B. 6-12 months
C. Indefinite
D. 6 weeks
Recommendation

For primary treatment of deep venous thrombosis or pulmonary embolism, the panel suggests short term (3-6 months) over long term anticoagulation (6-12 months) (conditional recommendation, moderate certainty)

**Long-term** compared with **short-term** anticoagulation for patients with VTE provoked by transient risk factor

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk with short-term</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.38 (0.85 to 2.23)</td>
<td>18 per 1,000</td>
</tr>
<tr>
<td>PE</td>
<td>0.66 (0.29 to 1.15)</td>
<td>50 per 1,000</td>
</tr>
<tr>
<td>DVT</td>
<td>0.50 (0.27 to 0.95)</td>
<td>117 per 1000</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1.46 (0.78 to 2.73)</td>
<td>13 per 1,000</td>
</tr>
</tbody>
</table>

*Results based on approx. 2.5 year follow up

**Remarks:**
For VTE provoked by transient risk factor, secondary prevention does not need to be considered

Quality of Evidence (GRADE): Low 🟢 Moderate 🟢 Strong 🟢

ASH CLINICAL PRACTICE GUIDELINES
VENOUS THROMBOEMBOLISM (VTE)
Case: back to our patient

Provoked (transient risk factor) PE in patient with cardiopulmonary disease

• Initial management:
  o Anticoagulation only (no thrombolysis, no compression stockings, no IVC filter)
  o DOAC over warfarin
  o Suspend ASA
  o Home treatment over hospital treatment

• Duration:
  o 3-6 months
  o No secondary prevention
    • Can resume ASA if otherwise indicated
Case epilogue:

Three years later while on ASA only, the patient undergoes an appendectomy for appendicitis. Seven days after surgery, the patient has new leg swelling and is diagnosed with an acute left leg DVT. ASA is suspended and he is restarted on a DOAC for 3 months.

For how long should he be treated with anticoagulation?

A. 3-6 months  
B. 6-12 months  
C. Indefinite  
D. 6 weeks
**Recommendation**

For patients who develop a DVT and/or PE provoked by a transient risk factor and have a history of a previous provoked thrombotic event the panel suggests stopping anticoagulation after completion of primary treatment (conditional recommendation, moderate certainty)

**Long-term** compared with **short-term** anticoagulation for patients with recurrent provoked VTE

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Risk with short-term</td>
<td>Risk difference with long-term anticoagulation</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.75 (0.49 to 1.13)</td>
<td>18 per 1,000</td>
</tr>
<tr>
<td>PE</td>
<td>0.29 (0.15 to 0.56)</td>
<td>29 per 1,000</td>
</tr>
<tr>
<td>DVT</td>
<td>0.20 (0.12 to 0.34)</td>
<td>117 per 1000</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>2.17 (1.40 to 3.35)</td>
<td>5 per 1,000</td>
</tr>
</tbody>
</table>
Case Conclusion

Provoked PE (transient risk factor) in patient with pre-existing cardiopulmonary disease

• Initial management:
  o Anticoagulation only (no thrombolysis, no compression stockings, no IVC filter)
  o DOAC over warfarin
  o Suspend ASA
  o Home treatment over hospital treatment

• Duration:
  o 3-6 months
  o No secondary prevention (can resume ASA if otherwise indicated)

• Recurrent VTE:
  o Reassess for initial management and primary treatment duration
  o No secondary prevention (in cases where first event is unprovoked, indefinite antithrombotic therapy is recommended)
Case 3: Provoked submassive PE (chronic risk factor)

56 year old female

**Medical History:** Inflammatory Bowel Disease, CKD (CrCl 14 ml/min)

**Medications:** Infliximab

**Seen in the Emergency Department with:** Presyncope after 2 days of SOB and chest pain.

Heart rate 104 beats per min
Respiratory rate 22 breaths per min
Oxygen saturation 98% on 2L
Blood pressure 150/90

**Troponin:** Troponin-T HS 250 ng/L

**CTPA:** Pulmonary embolism involving bilateral segmental arteries

**Bedside echo:** no clear evidence of right heart strain
This patient has extensive bilateral PE with positive troponin and radiographic findings of right heart strain. She is tachycardic but hemodynamically stable and responding well to IV fluids.

What initial management plan would you recommend:

A. Anticoagulation only
B. Systemic thrombolysis in addition to anticoagulation
C. Catheter-directed thrombolysis in addition to anticoagulation
D. IVC filter insertion in addition to anticoagulation
**Recommendation.**

For patients with PE with echocardiography and/or biomarkers compatible with right ventricular dysfunction but without hemodynamic compromise (submassive PE), the panel suggests anticoagulation alone over the routine use of thrombolysis in addition to anticoagulation (conditional recommendation, low certainty).

**Thrombolytic therapy in addition to anticoagulation versus anticoagulation alone:**

<table>
<thead>
<tr>
<th>Outcomes (Quality of Evidence)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk with ANTICOAGULATION ALONE</td>
</tr>
<tr>
<td>Mortality</td>
<td>RR 0.61 (0.40 to 0.94)</td>
<td>133 out of 1,000 (13.3%)</td>
</tr>
<tr>
<td>PE</td>
<td>RR 0.56 (0.35 to 0.91)</td>
<td>16 out of 1,000 (1.6%)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>RR 1.89 (1.46 to 2.46)</td>
<td>28 out of 1,000 (2.8%)</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>RR 3.17 (1.19-8.41)</td>
<td>3 per 1,000 (0.3%)</td>
</tr>
</tbody>
</table>

**Remarks:**
- Thrombolysis is reasonable to consider for younger patients with submassive PE at low risk for bleeding.
- Patients with submassive PE should be monitored closely for hemodynamic compromise.

**Hemodynamic compromise:**
sBP < 90 mm Hg, or a decrease in sBP ≥ 40 mm Hg from baseline.

*Quality of Evidence (GRADE): Low Moderate Strong*
Patient is started on IV UFH and bridged to warfarin (preferred due to CKD), what do you recommend for duration and type of antithrombotic therapy?

A. 3-6 months of anticoagulation then stop
B. 3-6 months of anticoagulation, then continue anticoagulant therapy for secondary VTE prevention indefinitely
C. 3-6 months of anticoagulation then switch to ASA for secondary VTE prevention
D. 6-12 months of anticoagulation then stop
Recommendation

After primary treatment for patients with DVT and/or PE provoked by a chronic risk factor, the panel suggests indefinite antithrombotic therapy over stopping anticoagulation (conditional recommendation moderate certainty)

**Long-term** compared with **short-term** anticoagulation for patients with VTE provoked by chronic risk factor

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality</strong></td>
<td>0.75 (0.49 to 1.13)</td>
<td>16 per 1,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 fewer deaths per 1,000 (8 fewer to 2 more)</td>
</tr>
<tr>
<td><strong>PE</strong></td>
<td>0.29 (0.15 to 0.56)</td>
<td>29 per 1,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>21 fewer PE per 1,000 (25 fewer to 13 fewer)</td>
</tr>
<tr>
<td><strong>DVT</strong></td>
<td>0.20 (0.12 to 0.34)</td>
<td>63 per 1000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 fewer DVT per 1,000 (56 fewer to 42 fewer)</td>
</tr>
<tr>
<td><strong>Major bleeding</strong></td>
<td>2.17 (1.40 to 3.35)</td>
<td>5 per 1,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 more bleeds per 1,000 (2 more to 12 more)</td>
</tr>
</tbody>
</table>

Chronic thrombotic risk factors include:
- Inflammatory bowel disease
- Autoimmune disease
- Active cancer
- Chronic immobility
- Chronic infections

*Results based on approx. 2 year follow up
Recommendation

For patients with DVT and/or PE who will continue to receive secondary prevention, the panel suggests using anticoagulation over aspirin (conditional recommendation, moderate certainty).

Aspirin compared with anticoagulation for patients with receiving secondary prevention for prior VTE

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk with anticoagulation</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.86 (0.31 to 2.35)</td>
<td>7 per 1,000</td>
</tr>
<tr>
<td>PE</td>
<td>3.10 (1.24 to 7.73)</td>
<td>5 per 1,000</td>
</tr>
<tr>
<td>DVT</td>
<td>3.15 (1.50 to 6.63)</td>
<td>8 per 1000</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>0.49 (0.12 to 1.95)</td>
<td>5 per 1,000</td>
</tr>
</tbody>
</table>

Quality of Evidence (GRADE): Low Moderate Strong
Case Conclusion

Provoked submassive PE (chronic risk factor)

• Initial management:
  o Anticoagulation only (no thrombolysis, no compression stockings, no IVC filter)
  o Consider admission to hospital

• Duration of anticoagulation
  o Indefinite antithrombotic therapy with anticoagulation rather than ASA
Other guideline recommendations that were not covered in this session

- Home treatment vs hospital treatment for patients with PE and low risk for complication
- Thrombolytic therapy plus anticoagulation vs anticoagulation alone for patients with PE and hemodynamic compromise
- Systemic vs. catheter-directed thrombolysis for DVT, PE
- Breakthrough VTE
- INR intensity on warfarin when being used as the anticoagulant for secondary prophylaxis
Future Priorities for Research

• Which patients with DVT or PE would benefit most from thrombolytic therapy and optimal strategy for administration

• Which patient populations would benefit most from the incorporation of ≥1 of prognostic scores, D-dimer testing, and/or ultrasound into the decision-making process concerning whether anticoagulant therapy should be continued after completion of the primary treatment phase of therapy.

• Impact of different chronic risk factors on the rate of recurrent VTE

• Which patients can safely use a lower-dose DOAC for secondary prevention

• The evaluation and management of patients who sustain breakthrough thromboembolic events

• Which patients should continue antiplatelet therapy when anticoagulant therapy is initiated and which anticoagulant agent(s) and dose(s) are safest when coadministered with antiplatelet therapy.

• Which patients would potentially benefit from the use of compression stockings.
In Summary: Back to our Objectives

1. Describe the *initial management* of patients with deep vein thrombosis (DVT) and pulmonary embolism (PE)

2. Describe recommendations for *duration of anticoagulation* after venous thromboembolism (VTE)

3. Describe recommendations for management of *recurrent VTE*
Acknowledgements

• ASH Guideline Panel team members
• Knowledge Synthesis team members
• McMaster University GRADE Centre
• Authors of this slide set: Zachary Liederman MD MScCH (University of Toronto), Eric K. Tseng MD MScCH (University of Toronto) and Thomas L. Ortel MD PhD (Duke University)

See more about the ASH VTE guidelines at www.hematology.org/VTEguidelines
Don’t miss our updated ASH VTE Guidelines Mobile App!